CLAIMS

We claim:

1. A method of promoting lipid mobilization in a human, the method comprising administering an insect adipokinetic hormone to the human in an amount effective to mobilize lipids in the human.

2. The method of claim 1, wherein the hormone has a molecular weight less than 2500.

3. The method of claim 1, wherein the hormone is a polypeptide having a pyroglutamate residue at its amino terminus.

4. The method of claim 1, wherein the hormone is a polypeptide having a blocked carboxyl terminus.

5. The method of claim 4, wherein the carboxyl terminus of the polypeptide is aminated.

6. The method of claim 1, wherein the hormone is a polypeptide that does not have internal disulfide bonds.

7. The method of claim 1, wherein the hormone is characterized in that its ability to promote lipid mobilization is not significantly inhibited by propanolol.

8. The method of claim 1, wherein the hormone is a polypeptide characterized in that:

i) it has a molecular weight less than 2500;

ii) it has a pyroglutamate residue at its amino terminus;

iii) it is aminated at its carboxyl terminus;

iv) it does note have internal disulfide bonds; and

v) its ability to promote lipid mobilization is not significantly inhibited by propanolol.

9. The method of claim 1, wherein the hormone has the chemical structure

$Xaa^1 - Xaa^2 - Xaa^3 - Xaa^4 - Xaa^5 - Xaa^6 - Xaa^7 - Xaa^8 - X - Z$,

wherein:

Xaa^1 is a pyroglutamate residue;

Xaa^2 is one of a leucine residue, an isoleucine residue, a valine residue, a phenylalanine residue, and a tyrosine residue;

Xaa^3 is one of an asparagine residue and a threonine residue;

Xaa^4 is one of a phenylalanine residue and a tyrosine residue;

Xaa^5 is one of a threonine residue and a serine residue;

Xaa^6 is one of a proline residue, a serine residue, a threonine residue, and an alanine residue;

Xaa^7 is one of glycine residue, an asparagine residue, a serine residue, an aspartate residue, a valine residue, and a tryptophan residue;

Xaa^8 is a tryptophan residue;

X is from 0 to 10 amino acid residues; and

Z is one of a hydrogen radical and a carboxyl terminus-blocking moiety.

10. The method of claim 9, wherein:

Xaa^2 is one of a leucine residue, and a valine residue;

Xaa^6 is a proline residue, a serine residue, and a threonine residue;

Xaa^7 is one of glycine residue, an asparagine residue, and a serine residue;

Xaa^8 is a tryptophan residue;

X is from 0 to 3 amino acid residues; and

Z is an ($-NH_2$) radical.

11. The method of claim 10, wherein Xaa^4 is a phenylalanine residue.

12. The method of claim 9, wherein:

X is 0 amino acid residues; and

Z is an ($-NH_2$) radical.

13. The method of claim 9, wherein X is a glycine residue.

14. The method of claim 13, wherein Z is an ($-NH_2$) radical.

15. The method of claim 9, wherein X has the chemical structure

$$Xaa^9 - Xaa10$$

wherein:

Xaa^9 is glycine; and

Xaa^{10} is one of a threonine residue, a glycine residue, a tryptophan residue, a serine residue, and an asparagine residue.

16. The method of claim 15, wherein Xaa^{10} is a threonine residue.

17. The method of claim 15, wherein Z is an ($-NH_2$) radical.

18. The method of claim 9, wherein X has the chemical structure

$$Xaa^9 - Xaa^{10} - Xaa^{11}$$

wherein:

Xaa^9 is glycine;

Xaa^{10} is one of a threonine residue, a glycine residue, a tryptophan residue, a serine residue, and an asparagine residue; and

Xaa^{11} is a lysine residue.

19. The method of claim 9, wherein X has the chemical structure

$$Xaa^9 - Xaa^{10} - Xaa^{11} - (Xaa^{12})_n$$

wherein

n is from 0 to 7

Xaa^9 is a glycine residue,

Xaa^{10}, when present, is one of a threonine residue, a glycine residue, a tryptophan residue, a serine residue, and an asparagine residue;

Xaa^{11}, when present, is a lysine residue; and

each Xaa^{12}, when present, is any amino acid residue.

20. The method of claim 9, wherein X is a glycine residue and Z is a hydrogen radical.

21. The method of claim 9, wherein the hormone is administered in an amount in the range from 100 milligrams to about 2 grams per day.

22. The method of claim 21, wherein the hormone is administered in an amount in the range from 200 milligrams to 1.0 gram per day.

23. The method of claim 1, wherein the hormone has the chemical structure

$$Xaa^1 - Xaa^{22} - Xaa^{23} - Xaa^{24} - Xaa^{25} - Xaa^{26} - Xaa^{27} - Xaa^{28} - X - Z,$$

wherein:

Xaa^1 is a pyroglutamate residue;

Xaa^{22} is an amino acid residue having a non-polar side chain;

Xaa^{23} is an amino acid residue having a non-ionic polar side chain;

Xaa^{24} is an amino acid residue having an aromatic side chain;

Xaa^{25} is an amino acid residue having a non-ionic polar side chain;

Xaa^{26} is any amino acid residue;

Xaa^{27} is any amino acid residue;

Xaa^{28} is an amino acid residue having an aromatic side chain;

X is from 0 to 10 amino acid residues; and

Z is one of a hydrogen radical and a carboxyl terminus-blocking moiety.

24. The method of claim 23, wherein:

Xaa^{26} is one of a proline residue, a serine residue, a threonine residue, and an alanine residue.

25. The method of claim 23, wherein:

Xaa^{27} is one of glycine residue, an asparagine residue, a serine residue, a glutamate residue, a valine residue, and a tryptophan residue.

26. The method of claim 23, wherein Z is an ($-NH_2$) radical.

27. The method of claim 26, wherein X is 0 amino acid residues.

28. The method of claim 23, wherein X is a glycine residue and Z is a hydrogen radical.

29. The method of claim 1, wherein the hormone is a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NOs: 1-40, wherein the amino-terminal glutamate residue of the polypeptide is a pyroglutamate residue, and wherein the carboxyl terminal residue of the polypeptide is amidated.

30. A method of promoting lipid mobilization in a human, the method comprising administering to the human, in an amount effective to mobilize lipids in the human, a compound having the chemical structure

$$Xaa^1 - Xaa^2 - Xaa^3 - Xaa^4 - Xaa^5 - Xaa^6 - Xaa^7 - Xaa^8 - X - Z,$$

wherein:

Xaa^1 is a pyroglutamate residue;

Xaa^2 is one of a leucine residue, an isoleucine residue, a valine residue, a phenylalanine residue, and a tyrosine residue;

Xaa^3 is one of an asparagine residue and a threonine residue;

Xaa^4 is one of a phenylalanine residue and a tyrosine residue;

Xaa^5 is one of a threonine residue and a serine residue;

Xaa^6 is one of a proline residue, a serine residue, a threonine residue, and an alanine residue;

Xaa^7 is one of glycine residue, an asparagine residue, a serine residue, an aspartate residue, a valine residue, and a tryptophan residue;

Xaa^8 is a tryptophan residue;

X is from 0 to 10 amino acid residues; and

Z is one of a hydrogen radical and a carboxyl terminus-blocking moiety.

31. A method of promoting lipid mobilization in a human, the method comprising administering to the human, in an amount effective to mobilize lipids in the human, a compound having the chemical structure

$$Xaa^1 - Xaa^{22} - Xaa^{23} - Xaa^{24} - Xaa^{25} - Xaa^{26} - Xaa^{27} - Xaa^{28} - X - Z,$$

wherein:

Xaa^1 is a pyroglutamate residue;

Xaa^{22} is an amino acid residue having a non-polar side chain;

Xaa^{23} is an amino acid residue having a non-ionic polar side chain;

Xaa^{24} is an amino acid residue having an aromatic side chain;

Xaa^{25} is an amino acid residue having a non-ionic polar side chain;

Xaa^{26} is any amino acid residue;

Xaa^{27} is any amino acid residue;

Xaa^{28} is an amino acid residue having an aromatic side chain;

X is from 0 to 10 amino acid residues; and

Z is one of a hydrogen radical and a carboxyl terminus-blocking moiety.

32. A method of promoting lipid mobilization in a human, the method comprising administering to the human a nucleic acid expression vector comprising a nucleic acid encoding a polypeptide having the chemical structure

$$Xaa^0 - Xaa^2 - Xaa^3 - Xaa^4 - Xaa^5 - Xaa^6 - Xaa^7 - Xaa^8 - X,$$

wherein:

Xaa^0 is one of a glutamate residue and a glutamine residue;

Xaa^2 is one of a leucine residue, an isoleucine residue, a valine residue, a phenylalanine residue, and a tyrosine residue;

Xaa^3 is one of an asparagine residue and a threonine residue;

Xaa^4 is one of a phenylalanine residue and a tyrosine residue;

Xaa^5 is one of a threonine residue and a serine residue;

Xaa^6 is one of a proline residue, a serine residue, a threonine residue, and an alanine residue;

Xaa^7 is one of glycine residue, an asparagine residue, a serine residue, an aspartate residue, a valine residue, and a tryptophan residue;

Xaa^8 is a tryptophan residue; and

X is from 0 to 10 amino acid residues.

33. A method of making a pharmaceutical composition for promoting lipid mobilization in a human, the method comprising

i) cyclizing the amino-terminal amino acid residue of a polypeptide having the chemical structure

$$Xaa^0 - Xaa^2 - Xaa^3 - Xaa^4 - Xaa^5 - Xaa^6 - Xaa^7 - Xaa^8 - X,$$

wherein:

Xaa^0 is one of a glutamate residue and a glutamine residue;

Xaa^2 is one of a leucine residue, an isoleucine residue, a valine residue, a phenylalanine residue, and a tyrosine residue;

Xaa^3 is one of an asparagine residue and a threonine residue;

Xaa^4 is one of a phenylalanine residue and a tyrosine residue;

Xaa^5 is one of a threonine residue and a serine residue;

Xaa^6 is one of a proline residue, a serine residue, a threonine residue, and an alanine residue;

Xaa^7 is one of glycine residue, an asparagine residue, a serine residue, an aspartate residue, a valine residue, and a tryptophan residue;

Xaa^8 is a tryptophan residue; and

X is from 0 to 10 amino acid residues

so that the polypeptide has a pyroglutamate residue at its amino terminus; and

ii) combining the polypeptide with a pharmaceutically acceptable carrier.

34. The method of claim 33, further comprising

iii) blocking the amino terminus of the polypeptide.

35. The method of claim 34, wherein the amino terminus is blocked by amidating the amino terminus.

36. A method of promoting weight loss in a human, the method comprising administering an insect adipokinetic hormone to the human in an amount effective to mobilize lipids in the human.

37. The method of claim 36, wherein the human is afflicted with obesity.

38. A method of suppressing the appetite of a human, the method comprising administering an insect adipokinetic hormone to the human in an amount effective to mobilize lipids in the human, whereby the human's appetite is suppressed.

39. A pharmaceutical composition for promoting weight loss in a human, the composition comprising an insect adipokinetic hormone and a pharmaceutically acceptable carrier.

40. A kit for promoting weight loss in a human, the kit comprising the pharmaceutical composition of claim 39 and an instructional material that describes use of the composition for promoting weight loss.

41. A method of identifying an agent effective for promoting lipolysis in humans, the method comprising

i) derivatizing a compound having the chemical structure

$$Xaa^1 - Xaa^2 - Xaa^3 - Xaa^4 - Xaa^5 - Xaa^6 - Xaa^7 - Xaa^8 - X - Z,$$

wherein:

Xaa^1 is a pyroglutamate residue;

Xaa^2 is one of a leucine residue, an isoleucine residue, a valine residue, a phenylalanine residue, and a tyrosine residue;

Xaa^3 is one of an asparagine residue and a threonine residue;

Xaa^4 is one of a phenylalanine residue and a tyrosine residue;

Xaa^5 is one of a threonine residue and a serine residue;

Xaa^6 is one of a proline residue, a serine residue, a threonine residue, and an alanine residue;

Xaa^7 is one of glycine residue, an asparagine residue, a serine residue, an aspartate residue, a valine residue, and a tryptophan residue;

Xaa^8 is a tryptophan residue;

X is from 0 to 10 amino acid residues; and

Z is one of a hydrogen radical and a carboxyl terminus-blocking moiety

to form a polypeptide derivative; and

ii) assessing the ability of the derivative to mobilize lipids, whereby ability of the derivative to mobilize lipids is an indication that the derivative is an agent effective for promoting lipolysis in humans.

42. The method of claim 41, wherein the ability of the derivative to mobilize lipids is assessed in vitro in human adipocytes.

43. The method of claim 41, wherein the ability of the derivative to mobilize lipids is assessed in the presence and absence of a beta adrenergic receptor antagonist, whereby

failure of the antagonist to significantly inhibit the ability of the derivative to mobilize lipids is an indication that the derivative is an agent effective for promoting lipolysis in humans.

44. A method of assessing the ability of a test compound to modulate lipid mobilization in a human cell, the method comprising assessing the ability of an insect AKH to mobilize lipids in the cell in the presence and absence of the test compound, whereby a difference between

i) the ability of the insect AKH to mobilize lipids in the cell in the presence of the test compound and

ii) the ability of the insect AKH to mobilize lipids in the cell in the presence of the test compound

is an indication that the test compound is able to modulate lipid mobilization in the cell.

45. A method of promoting lipid mobilization in a human, the method comprising administering an insect adipokinetic hormone to the human in an amount effective to mobilize lipids in the human, wherein the hormone has the chemical structure

$$Xaa^1 - Xaa^3 - Xaa^4 - Xaa^5 - Xaa^6 - Xaa^7 - Xaa^8 - Z,$$

wherein:

Xaa^1 is a pyroglutamate residue;

Xaa^3 is one of an asparagine residue and a threonine residue;

Xaa^4 is one of a phenylalanine residue and a tyrosine residue;

Xaa^5 is one of a threonine residue and a serine residue;

Xaa^6 is one of a proline residue, a serine residue, a threonine residue, and an alanine residue;

Xaa^7 is one of glycine residue, an asparagine residue, a serine residue, an aspartate residue, a valine residue, and a tryptophan residue;

Xaa^8 is a tryptophan residue; and

Z is one of a hydrogen radical and a carboxyl terminus-blocking moiety.

46. A method of promoting lipid mobilization in a human, the method comprising administering an insect adipokinetic hormone to the human in an amount effective to mobilize lipids in the human, wherein the hormone has the chemical structure

$$Xaa^1 - Xaa^3 - Xaa^4 - Xaa^5 - Xaa^6 - Lys - Z,$$

wherein:

Xaa^1 is a pyroglutamate residue;

Xaa^3 is one of an asparagine residue and a threonine residue;

Xaa^4 is one of a phenylalanine residue and a tyrosine residue;

Xaa^5 is one of a threonine residue and a serine residue;

Xaa^6 is one of a proline residue, a serine residue, a threonine residue, and an alanine residue; and

Z is one of a hydrogen radical and a carboxyl terminus-blocking moiety.